243S and LRT7. The resulting products were digested with BbsI and BamHI and an ~300 bp fragment was gel purified and ligated to BbsI/BamHI-digested phPS1 to generate phPS1C410Y.

Please replace the paragraph beginning on page 54, line 13 with the following paragraph:

PS2: Full-length cDNA encoding human PS2 was generated by RT-PCR of total human brain RNA using a sense primer, huAD4-ATGF (CCGGTACCAAGTGTTCGTGGTGCTTCC, SEQ ID NO:26) and antisense primer, hAD4-stopR (CCGTCTAGACCTCAGATGTAGAGCTGATG, SEQ ID NO:27). PCR products were digested with Asp718 and XbaI and ~1.4 kB hPS2 cDNA were gel isolated and ligated to a vector fragment from expression plasmid pCB6 (17) previously digested with Asp718 and XbaI to generate phPS2. The insert was sequenced in its entirety using a Sequenase kit (U.S. Biochemical Corp., Cleveland, OH).

REMARKS

In the September 3, 2002 Notice, the Examiner stated that the application fails to comply with the sequence rules. The Examiner stated that applicants must provide (a) an initial computer readable form (CRF) of the sequence listing, (b) an initial paper copy of the sequence listing and an amendment directing its entry into the application, and (c) a statement that the content of the sequence information recorded in computer readable form is identical to that of the paper sequence listing and, where applicable, includes no new matter, as required by 37 C.F.R. 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

In response, applicants submit (a) a paper copy of the Sequence Listing attached hereto as **Exhibit B**, (b) a CRF of the sequence listing, and (c) a statement in accordance with 37 C.F.R. §1.821(f) attached hereto as **Exhibit C**, certifying that (i) the CRF and written sequence listing contain the same sequence information, and (ii) the sequence listing contains no new matter.

Finally, pursuant to the requirements of 37 C.F.R. §1.121, applicants annex hereto as **Exhibit D** a copy of the amended paragraphs of the specification marked-up to show the changes made herein relative to the previous version thereof.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
U.S. Patent and Trademark Office
Box Sequence, P.O. Box 2327
Arlington, VA 22202

10/3/02

Alan J. Morrison
Reg. No. 37,399

Date

John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

Marked-up version of amended specification

The paragraph beginning on page 52, line 31:

PS1: Full-length human PS1 cDNA and cDNA encoding the PS1 A246E substitution were generated by RT-PCR of cytoplasmic RNA isolated from skin fibroblasts of a patient harboring the A246E mutation (NIA Cell Repository #AG06848B) using a sense primer, hAD3-ATG-Kpn (GGGGTACCATGACAGAGTTACCTGCAC, SEQ ID NO:10), and antisense primer, hAD3-R-3'UTR (CCGGGATCCATGGGATTCTAACCGC, SEQ ID NO:11). PCR products were digested with Asp718 and BamHI and ~1.4 kB hPS1 cDNAs were gel purified and ligated to Bluescript KS+ vector (Stratagene, La Jolla, CA.) previously digested with Asp718 and BamHI, to generate phPS1 and phPS1A246E. The cDNAs were sequenced in their entirety using a Sequenase kit (U.S. Biochemical Corp., Cleveland, OH).

The paragraph beginning on page 53, line 11:

For M146L, primer pairs were hAD3-M146LF (GTCATTGTTGTCCTGACTATCCTCCTG, SEQ ID NO:12) /hAD3-R284 (GAGGAGTAAATGAGAGCTGG, SEQ ID NO:13) and hAD3-M146LR (CAGGAGGATAGTCAGGACAACAATGAC, SEQ ID NO:14) /hAD3-237F (CAGGTGGTGGAGCAAGATG, SEQ ID NO:15). PCR products from each reaction were gel purified, combined and subject to a second round of PCR with primers hAD3-237F and

hAD3-R284. The resulting product was digested with KasI and PflMI and an ~300 bp gel purified fragment was ligated to KasI/PflMI-digested phPS1 to generate phPS1MI46L. For H163R, primer pairs were hAD3-H163RF (CTAGGTCATCCGTGCCTGGC, SEQ ID NO:16) /hAD3-R284 and hAD3-H163RR (GCCAGGCACGGATGACCTAG, SEQ ID NO:17) /hAD3-237F. PCR products from each reaction were gel purified, combined and subject to a second round of PCR with primers hAD3-237F and hAD3-R284. The resulting products were digested with KasI and PflMI and a gel-purified ~300 bp fragment was ligated to KasI/PflMI-digested phPS1 to generate phPS1H163R.

The paragraph beginning on page 53, line 28:

For L286V, primer pairs were hAD3-L286VF (CGCTTTTTCCAGCTGTCATTTACTCC, SEQ ID NO:18) / hAD3-RL-GST (CCGGAATTCTCAGGTTGTGTTCCAGTC, SEQ ID NO:19) and hAD3-L286VR (GGAGTAAATGACAGCTGGAAAAAGCG, SEQ ID NO:20) / hAD3 -F146 (GGATCCATTGTTGTCATGACTATC, SEQ ID NO:21). PCR products from each reaction were gel purified, combined and subject to a second round of PCR with primers hAD3-F146 and hAD3-RL-GST. The resulting products were digested with PflMI and BbsI and a gel purified ~480 bp fragment was ligated to PflMI/BbsI-digested phPS1 to generate phPS1L286V.

The paragraph beginning on page 53, line 39:

For C410Y, primer pairs were hAD3-C410YF (CAACCATAGCCTATTTCGTAGCC, SEQ ID NO:22) /LRT7

(GCCAGTGAATTGTAATAGGACTCACTATAGGGC, SEQ ID NO:23) and hAD3-C410YR (GGCTACGAAATAGGCTATGGTTG, SEQ ID NO:24) /hAD3-243S (CCGGAATTCTGAATGGACTGCGTG, SEQ ID NO:25). PCR products from each reaction were gel purified, combined and subject to a second round of PCR with primers hAD3-243S and LRT7. The resulting products were digested with BbsI and BamHI and an ~300 bp fragment was gel purified and ligated to BbsI/BamHI-digested phPS1 to generate phPS1C410Y.

The paragraph beginning on page 54, line 13:

PS2: Full-length cDNA encoding human PS2 was generated by RT-PCR of total human brain RNA using a sense primer, huAD4-ATGF (CCGGTACCAAGTGTTCGTGGTGCTTCC, SEQ ID NO:26) and antisense primer, hAD4-stopR (CCGTCTAGACCTCAGATGTAGAGCTGATG, SEQ ID NO:27). PCR products were digested with Asp718 and XbaI and ~1.4 kB hPS2 cDNA were gel isolated and ligated to a vector fragment from expression plasmid pCB6 (17) previously digested with Asp718 and XbaI to generate phPS2. The insert was sequenced in its entirety using a Sequenase kit (U.S. Biochemical Corp., Cleveland, OH).

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OCT 07 2002
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Dkt. 0575/48231-A-PCT-US/JPW/AJM/MML

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Iva Greenwald and Diane Levitan

Serial No.: 09/043,944

Filed : March 27, 1998

For : IDENTIFICATION OF SEL-12 AND USES THEREOF

1185 Avenue of the Americas
New York, New York 10036
October 3, 2002

U.S. Patent and Trademark Office
Box Sequence, P.O. Box 2327
Arlington, VA 22202

Sir:

STATEMENT IN ACCORDANCE WITH 37 C.F.R. §1.821(f)

In accordance with 37 C.F.R. §1.821(f), I hereby certify that the computer readable form containing the nucleic acid and/or amino acid sequences required by 37 C.F.R. §1.821(e) and submitted herewith in connection with the above-identified application contains the same information as the written "Sequence Listing" submitted herewith as Exhibit B, and includes no new matter.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Muriel M. Liberto
c/o Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

JPW

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09043944	10/06/2000	Greenwald, I. Et al.	48231-A-PCT-US

9/3/2002
30 Days: 10/3/2002
2 Mos: 11/3/2002
3 Mos: 12/3/2002
4 Mos: 1/3/2003
5 Mos: 2/3/2003
6 Mos: 3/3/2003 SMC

EXAMINER	
Samuel Wei Liu	
ART UNIT	PAPER NUMBER
1653	

Please find below a communication from the EXAMINER in charge of this application

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN 30 days FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ExaminerSamuel Wei Liu whose telephone number is (703) 306-3483. If the examiner cannot be reached, inquiries can be directed to Supervisory Patent Examiner Christopher Low whose telephone number is (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Application No.: 09043944

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

RECEIVED
OCT 10 2002
TECH CENTER 1600/2900

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/043,944	10/06/2000	Iva Greenwald	48231-A-PCT-US	7588

7590 09/03/2002

John P White
Cooper & Dunham
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
LIU, SAMUEL W	
ART UNIT	PAPER NUMBER
1653	14

DATE MAILED: 09/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.